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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,564	10/20/2003	Ellen-Marie Gottschalk	35635-94974	8408

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/689,564	GOTTSCHALK ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *19-22 and 25-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,23,24 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/29/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending.

Election/Restrictions

Claims 19-22 and 25-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups II-IV, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 21, 2006.

Applicant's election without traverse of Group I, claims 1-18, 23, 24 and 31, in the reply filed on April 21, 2006 is acknowledged.

Information Disclosure Statement

The reference A15, JP07143881, on the information disclosure statement filed 1/29/04 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

The disclosure is objected to because of the following informalities: because throughout the specification "creatinine deaminase" is typed as "creatinine deiminase".

Appropriate correction is required.

Claim Objections

Claims 1-18, 23, 24 and 31 are objected to because of the following informalities: the claims recite "creatinine deaminase" instead of "creatinine deiminase".

Claim 31 is objected to as dependent from the non-elected claim 19.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18, 23, 24 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a nucleic acid sequence encoding a polypeptide having creatinine deaminase activity as shown in SEQ ID NO:1 or a fragment or a derivative thereof or a sequence capable of hybridizing thereto. The rejection is over "a derivative" of SEQ ID NO:1 and a sequence capable of hybridizing to SEQ ID NO;1, a fragment or derivative thereof under undefined, assuming low, hybridization conditions. The term

"derivative" is defined in the specification as a nucleic acid sequence comprising "an individual or multiple nucleotide substitution, deletion and/or addition in the nucleic acid sequence" (page 20, lines 25-30). Since the number of possible nucleotide substitution, deletion and/or addition is not limited, it reads on any nucleic acid encoding a polypeptide having creatinine deaminase activity. Since the hybridization conditions are not limited and/or because the claim includes nucleic acids that hybridize to a derivative of SEQ ID NO:1, it reads on any nucleic acid encoding a polypeptide having creatinine deaminase activity. Therefore, the claim 1 encompasses the genus of nucleic acid sequences defined by function only. With regard to claim 3 it reads on any gene encoding a polypeptide having creatinine deaminase activity from *Tissierella creatinini.*

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical

characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification the genus of the nucleic acid sequence encoding a polypeptide having creatinine deaminase activity is represented by a nucleic acid of SEQ ID NO:1 from *Tissierella creatinini* encoding creatinine deaminase of SEQ ID NO:2. The specification fails to describe any other representative species of nucleic acids encoding a polypeptide having creatinine deaminase activity by any identifying characteristics or properties other than the functionality of encoding a polypeptide having creatinine deaminase activity.

The specification fails to define those structural features of nucleic acids encoding a polypeptide having creatinine deaminase activity that are commonly possessed by members of the genus that distinguish them from others. The specification fails to provide the structure and function correlation common to all members of the genus of nucleic acids encoding a polypeptide having creatinine deaminase activity. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention at the time of filing.

Claims 2-18, 23, 24 and 31 are included in this rejection as dependent from claim 1.

Claims 1-18, 23, 24 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid of SEQ ID NO:1 and a fragment thereof encoding a polypeptide having creatinine deaminase activity, does not reasonably provide enablement for a derivative of said nucleic acid sequence or a nucleic acid sequence that hybridizes thereto under undefined (low stringency) conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass nucleic acids encoding a polypeptide having creatinine deaminase activity and having an undefined, possibly low" percent identity to SEQ ID NO:1 because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting creatinine deaminase activity of the polypeptide of the instant invention; (B) the general tolerance of creatinine deaminases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid

residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, beyond that provided in order to make a nucleic acid encoding a polypeptide having creatinine deaminase activity and having an undefined, possibly low" percent identity to SEQ ID NO:1 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is confusing because by definition creatinine deaminase does not deaminate cytosine.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

the claimed invention is directed to non-statutory subject matter.

Claims 1-5, 14, 15, 17 and 18 are rejected under 35 U.S.C. 101 because they are drawn to a nucleic acid having the sequence of SEQ ID NO:1 and a host comprising thereof. *Tissierella creatinini* is a host cell comprising said nucleic acid. As a product of Nature said nucleic acid and a host cell comprising/expressing thereof are unpatentable. Amending the claims or claim 1 to recite "An isolated or purified nucleic acid", for example, would obviate this rejection.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Gottschalk, E. M., Hippe, H., Patzke, F. (1991) Clin. Chim. Acta 204: 223-238 (form PTO-1449 filed 1/29/04, reference A.1) describe purification to apparent homogeneity the creatinine deaminase from *Tissierella creatinini* (specification, page 20, lines 34-37).

Patent EP 1325958-A1 (July 09, 2003) describes the instant invention, including SEQ ID NOs: 1 and 2. It is not considered as the prior art under 35 U.S.C 102(a) because it has the same 4 inventors as the instant application (Gottschalk et al.). The filing date of the instant application is October 20, 2003.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652